



Seafood allergies: Fish and shellfish

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INTRODUCTION — Seafood allergy is the most common food allergy in adults and among the six most prevalent food allergies in young children [1].

The term "seafood" encompasses the following:

- Vertebrate finned fish, such as salmon, tuna, and cod
- Crustaceans, such as shrimp, prawn, crab, lobster, and crawfish
- Mollusks, such as squid, snails, and bivalves (scallops, clams, oysters, mussels, and others)

The term "shellfish", a subset of seafood, includes crustaceans and mollusks.

Seafood allergies are immunologic responses to proteins in these foods, and include IgE antibody-mediated allergy as well as other allergic syndromes [2-5]. They are distinct from adverse reactions due to toxins or infectious contaminants, which are not immune-based. (See "[Marine toxins](#)".)

In this topic review, the epidemiology, pathogenesis, clinical features, diagnosis, and management of seafood allergies will be presented. Issues of cross-reactivity among different forms of seafood are also addressed. General discussions of food allergy are presented separately in appropriate topic reviews.

EPIDEMIOLOGY

General population — Allergies to seafood are estimated to affect 1 to 2 percent of the adult population and less than 1 percent of children [6-9]. Allergy to shellfish is among the leading causes of food allergy in adults, and the most common cause of food-allergic emergency department visits [10].

Several large studies have provided estimates of prevalence [6-8,11]. One multinational survey of 17,280 adults (aged 20 to 44 years) from 15 countries questioned participants about foods that "nearly always" caused "illness" or "trouble" [7]. Shrimp, oyster, and fish were implicated by 2.3, 2.3, and 2.2 percent, respectively. In a random calling telephone survey in Canada, probable shellfish allergy was reported for 0.5 percent of children and 1.7 percent of adults [8]. The same study found rates of fish allergy to be 0.2 percent of children and 0.6 percent of adults.

Internationally, patterns of seafood consumption likely influence the prevalence of specific fish and shellfish allergies. As examples, allergy to whelk is seen in Korea, where this mollusk is a popular form of seafood, and barnacle allergy has been reported in the Portuguese population [12,13]. A random calling survey in Singapore found a reported rate of shellfish allergy of 7.2 percent in 4 to 6 year olds and 11.6 percent in 14 to 16 year olds; applying features of a convincing history reduced these rates to 1.2 percent and 5.2 percent, respectively [14]. However, these rates are higher than similar studies from the US and Canada [6,8].

An American study estimated the prevalence of seafood allergy using a nationwide, cross-sectional, telephone survey, in which a standardized questionnaire was administered to households chosen by randomly-generated phone numbers [6]. Criteria were established in advance to define seafood allergy by either a convincing history of symptoms (eg, urticaria, angioedema, trouble breathing, oral pruritus, or throat closing) or a diagnosis of allergy by a clinician. This study did not attempt to determine a rate of isolated gastrointestinal reactions to seafood. A total of 5529 households completed the survey (67.3 percent participation rate), representing a census of 14,948 individuals. Fish or shellfish allergy defined by established criteria was reported in 6 percent of households and among individuals as follows: 2.3 percent for any seafood allergy, 2 percent for shellfish, 0.4 percent for fish, and 0.2 percent for both fish and shellfish.

This study also revealed the following findings:

- Prevalence rates in children were significantly lower than those in adults in all categories, as follows: any seafood allergy (0.6 versus 2.8 percent), shellfish (0.5 versus 2.5 percent), and fish (0.2 versus 0.5 percent). Boys were affected more often than girls.
- In adults, the gender trend was reversed and rates in females were significantly higher than in males for both shellfish allergy (2.6 versus 1.5 percent) and fish allergy (0.6 versus 0.2 percent).
- The highest rates of seafood allergy were reported by African Americans, with

shellfish reported as the leading cause.

- The most common reported fish allergies, in order of decreasing frequency, were: salmon, tuna, catfish, cod, flounder, halibut, trout, and bass.
- The most common reported shellfish allergies, in decreasing frequency, were: shrimp, crab, lobster, clam, oyster, and mussel.

Referral populations — Seafood allergy accounts for up to one-third of serious allergic reactions to food in patients referred for allergy evaluations. Studies are relatively consistent around the world [[15-20](#)].

PATHOGENESIS — The major allergenic proteins in seafood that are responsible for IgE-mediated reactions have been identified. Persons with seafood allergy may react to these and/or other seafood proteins [[21](#)]:

- Parvalbumins are important allergens in fish [[22](#)].
- Tropomyosins are major allergens in shellfish and are also present in other arthropods (ie, dust mites, cockroaches), accounting for cross-reactivity between these groups [[23,24](#)]. (See '[Cross-reactivity with non-food allergens](#)' below.)
- In shrimp, the muscle proteins myosin light chain and sarcoplasmic calcium-binding protein are other prominent allergens [[25,26](#)].

The pathogenesis of non-IgE mediated seafood allergy is unclear. A syndrome that clinically resembles protein-induced enterocolitis has been described in both children and adults. (See '[Non IgE-mediated reactions](#)' below.)

CLINICAL FEATURES

IgE-mediated reactions — IgE-mediated allergic reactions are the most commonly described type of allergic reactions to seafood ingestion. These may present as generalized reactions, asthmatic reactions in response to occupational or household exposures, or as food-dependent, exercise-induced anaphylaxis.

IgE-mediated reactions are rapid in onset (usually within minutes to an hour after ingestion) and extra-gastrointestinal manifestations, such as urticaria, angioedema, respiratory symptoms, and laryngeal edema, are common ([table 1](#)). These can range in severity from mild to life threatening anaphylaxis; severe reactions are not uncommon [[2,27-29](#)]. The clinical features of IgE-mediated reactions are discussed in more detail elsewhere. (See '[Clinical manifestations of food allergy: An overview](#)'.)

Occupational and household exposures involving inhalation of cooking or processing

vapors may cause asthma [4,30,31]. (See "[Occupational asthma: Pathogenesis](#)".)

Food-dependent, exercise-induced anaphylaxis to seafood has also been reported. In this condition, the food causes symptoms only if ingestion is followed soon after by exercise or exertion, but is tolerated in the absence of exertion. Wheat products and seafood are the two most frequently implicated foods in this disorder [32]. (See "[Clinical manifestations of food allergy: An overview](#)".)

Severity — IgE-mediated fish and shellfish allergies can vary from mild to severe. In the US prevalence study, 60 to 70 percent of respondents experienced urticaria/angioedema, and over one-half reported dyspnea or throat tightness [6]. Consistent with this, approximately one-half of reactions prompted evaluation by a clinician or care in an emergency room. Despite the severe symptoms, administration of epinephrine was provided to only 16 percent of individuals treated in medical settings.

Several deaths from seafood allergy have been recorded. In a registry of food-induced fatal anaphylaxis comprised primarily of children, 1 of 32 deaths was due to fish, and in a report of seven deaths, one was reported to crab and one to fish [27,28]. In a United Kingdom registry of fatalities from anaphylaxis, 3 of 33 fatalities to a known food were caused by seafood [33].

Non IgE-mediated reactions — There are several other reactions to seafood exposure that are not IgE-mediated. These include:

- Food protein-induced enterocolitis in children, a non-IgE mediated allergic reaction
- An enterocolitis-like reaction in adults
- Contact dermatitis in those with occupational and household skin exposure

Gastrointestinal reactions — Food protein-induced enterocolitis has been described in children in response to fish, although there is a paucity of data on this entity. In the largest series of 14 children diagnosed between the ages of 9 and 12 months of age, symptoms consisted of vomiting, diarrhea, or both [34]. Three presented with a sepsis-like picture. Reactions occurred from a few minutes to up to six hours after ingestion. Skin prick tests were negative in all patients, and fish-specific serum IgE was positive in just one patient. Nine had the reactions confirmed by oral challenge. Four of these children eventually became tolerant of the causal food. Protein-induced enterocolitis in children is presented in more detail separately. (See "[Food protein-induced proctitis/colitis, enteropathy, and enterocolitis of infancy](#)".)

Seafood may also cause an enterocolitis-like disorder in adults, with delayed onset

of nausea, crampy abdominal pain, and protracted vomiting or diarrhea [1]. This appears to be primarily reported in response to mollusks. Adults typically present after having experienced this on several occasions, reporting that they had attributed the first one or two reactions to possible food poisoning. Indeed, these reactions clinically mimic diarrhetic shellfish poisoning (DSP), beginning one to six hours after ingestion and resolving within a few hours to three days, depending on severity. (See '[Differential diagnosis](#)' below.)

The etiology of these enterocolitis-like reactions in adults is unclear. Their repeated occurrence in certain individuals suggests either that some persons are more susceptible to toxic components in these foods, or that this reaction represents a form of allergy. There are very few studies of the pathogenesis of these reactions, although one study of adults with isolated gastrointestinal symptoms to various types of seafood included six patients who reacted repeatedly to oyster, in whom specific IgE was generally undetectable [35]. No formal information about epidemiology, range of severity, or prognosis is available, and there are no data to guide informed recommendations about this type of reaction. (See '[Delayed gastrointestinal reactions](#)' below.)

Allergic contact dermatitis — Allergic contact dermatitis can result from occupational skin exposure to seafood, in food handlers, for example [4,31]. Disruption of the skin barrier has been implicated as a risk factor for the development of this condition in exposed workers.

Age of onset and natural course — In the American prevalence survey reviewed previously, allergy developed in adulthood for 40 and 60 percent of individuals with fish and shellfish allergy, respectively [6]. Fifty-eight percent reported multiple reactions, with two to five episodes being typical [6]. Fifteen to 20 percent of people experienced more than six reactions [6].

Seafood allergy is considered to be persistent in most cases [34,36,37]. In a study evaluating IgE binding to various epitopes of major shrimp allergens, children showed stronger and more diverse IgE binding than adults, implying the allergy may wane with time. [38]. In the American telephone-based survey, only 3 to 4 percent of individuals with seafood allergy reported developing tolerance over time [6]. However, loss of fish allergy during childhood or in adulthood has been reported, although the extent to which this occurs is not well studied [37,39]. Recurrence of fish allergy after tolerance has also been reported [40].

DIAGNOSIS — A general discussion of the diagnosis of food allergy is presented elsewhere. A summary of this information, with a focus on those aspects that are most relevant to the diagnosis of seafood allergy, is provided below. (See "[History and physical examination in the patient with possible food allergy](#)" and "[Diagnostic tools for food allergy](#)".)

With the exception of in vitro immunoassays for specific IgE (which are commonly referred to as IgE RAST tests), other diagnostic allergy procedures, including skin testing and food challenges, should be performed by allergy specialists with training in the management of serious allergic reactions.

IgE-mediated reactions — For suspected IgE-mediated reactions, the history of an immediate reaction consisting of typical allergic symptoms, supported by positive tests for specific IgE antibodies, is sufficient to establish a diagnosis. Either skin prick tests or in vitro tests for IgE are usually performed initially. (See ["History and physical examination in the patient with possible food allergy"](#) and ["Diagnostic tools for food allergy"](#).)

The positive predictive value of skin prick testing with commercial seafood extracts and IgE immunoassays has not been compared to clinical reactivity in appropriate populations using oral food challenges. This is true for seafood and for most foods.

However, the negative predictive value of skin prick testing with commercial food extracts is generally high. In our clinic, we have found that negative skin tests with commercial seafood extracts that are in accordance with the clinical history are usually reliable. If there is uncertainty or the clinician has limited experience with a specific commercial extract, the actual food can be used for skin testing instead.

If the history is suggestive of allergy, and one or both forms of testing are negative, then it is useful to repeat skin testing using the implicated seafood, prepared in a manner similar to the exposure that caused the reaction (eg, raw if sushi caused the reaction). (See ["Diagnostic pitfalls"](#) below.)

In each case of diagnosed seafood allergy, possible allergy to cross-reactive fish or shellfish must be addressed. (See ["Cross-reactivity"](#) below and ["Eating other seafood"](#) below.)

If the history and/or IgE test results do not clearly indicate an allergy, then clinician-supervised oral food challenges would be required to exclude the diagnosis. The use of challenges in the diagnosis of food allergy is presented separately. (See ["Oral food challenges for diagnosis and management of food allergies"](#).)

Asthma — The diagnosis of suspected occupational asthma due to seafood allergy, which is also IgE-mediated, involves skin prick testing, pulmonary function testing, and possible bronchoprovocation challenge. Occupational asthma is discussed in more detail separately. (See ["Occupational asthma: Clinical features and diagnosis"](#).)

Other reactions — IgE tests are expected to be negative if the symptoms do not suggest an IgE-mediated reaction, such as delayed gastrointestinal reactions or

contact dermatitis.

- The diagnosis is confirmed by challenge in the case of food protein-induced enterocolitis in children. (See "[Food protein-induced proctitis/colitis, enteropathy, and enterocolitis of infancy](#)".)
- The diagnosis of enterocolitis in adults would also require challenge, although patients who have experienced these reactions on several occasions may decline, understandably. Diagnosis based upon history alone is reasonable in cases of recurrent reactions, as this essentially rules out incidental poisoning or bacterial contamination.
- In cases of contact dermatitis, patch testing with a preparation of the seafood in question may be informative, although such testing is not standardized. (See "[Overview of dermatitis](#)".)

Diagnostic pitfalls — There are several additional factors that can make the diagnosis of seafood allergy challenging ([table 2](#)). Digestion, various processing methods (heating/canning), and preparation issues (eg, which part of the fish is eaten) may influence the amount of relevant allergen in the final meal, as demonstrated by the following studies:

- Studies suggest that fish preparation methods (eg, boiling versus frying versus eating raw) may impact the allergenicity of fish in different ways [[41](#)]. Also, the impact of these factors can also vary among species of fish.
- During oral food challenges in children, it was observed that children passed food challenges to lyophilized fish in capsules but reacted to fresh fish [[42](#)].
- Digestion can also reduce the potential allergenicity of fish allergen, and may result in variable clinical outcomes depending upon, for example, stomach acidity [[43-45](#)].
- The part of the fish ingested can have different levels of the major allergen, such that dark or red muscle may lack the allergen compared to white muscle [[46,47](#)]. It is also possible to be allergic to caviar (fish roe) but not fish [[48](#)].

Because of these variables, it is important to repeat skin testing using the same seafood, prepared in a similar manner to that which caused the reaction, whenever a convincing clinical history cannot be readily validated by routine testing.

Allergy to canned tunafish — Patients who react to fresh tuna and salmon will typically tolerate canned versions of these fish, presumably because of modification of allergens during processing. Because of this, commercial extracts and possibly fresh foods may be required for skin testing patients who reacted to fresh forms of

these fish. If an individual has reacted to fresh tuna or salmon and is interested in eating the canned form, additional testing and supervised oral food challenges are suggested.

Conversely, allergy specifically to canned tuna has been described [49]. In addition, some brands of canned tuna contain soy or milk proteins that are added during processing, and this possibility should also be considered in patients who react only to canned tuna (and may apply to other canned fish).

Anisakis — Allergy to the fish parasite *Anisakis simplex* represents another potential diagnostic dilemma [50-53]. *Anisakis simplex* is a nematode that infects fish worldwide and can cause several health issues in humans. Humans are accidental hosts who can become transiently infected as a result of eating the raw or undercooked flesh of infected fish (typically herring, hake, black plaice and cod) [54]. Deep freezing and rethawing of fish kills the parasite [55]. Some countries (including the United States) have legislation requiring that any fish intended for consumption raw must be deep frozen for specified time periods (which differ depending on the temperatures used) [55]. However, this may not be strictly enforced [56]. The majority of recent cases of *Anisakis* reactions have been reported by Spanish investigators [53].

One manifestation of *Anisakis* allergy is a generalized reaction involving urticaria, angioedema, abdominal pain, and/or anaphylaxis, which develops as the live larvae penetrate the gastric mucosa [57,58]. Gastrointestinal symptoms may be minimal or absent and a delay in the onset of symptoms of between 2 and 24 hours is typical [59,60]. This delay between consumption of raw fish and onset of symptoms can be an important diagnostic clue to the presence of *Anisakis* allergy [53].

A major allergenic protein (Ani s 7) in *Anisakis* species has been identified, although a test for the presence of specific IgE to Ani s 7 is not yet commercially available [61]. It appears that parasite larvae must be viable to induce the reaction described previously, as neither skin testing with whole body extracts nor oral challenge with lyophilized parasites reproduces symptoms [51,52,62]. Excretory or secretory proteins produced by the live larvae have been implicated as possible allergens [52,59].

Anisakis allergy likely contributes to occupational respiratory allergy and contact dermatitis in fish processing workers. In one study, sensitization to *Anisakis* was as common as that to fish [62]. However, it is currently not clear what other clinical syndromes can be correctly attributed to *Anisakis* allergy. The optimal approach to skin testing is also uncertain, although prick-by-prick skin testing with live larvae appears to be most consistently positive in patients with urticaria/angioedema or anaphylaxis [59]. In contrast, the diagnosis of acute infection with *Anisakis* can be confirmed with serologic and gastroenterological tests and is presented elsewhere.

(See ["Miscellaneous nematodes"](#).)

DIFFERENTIAL DIAGNOSIS

Scombroid poisoning — The primary masquerader of IgE-mediated reactions is scombroid fish poisoning [63,64]. In 1999, 19 cases of scombroid poisoning were reported in the United States [5], although many more cases likely go undetected. The epidemiology, clinical manifestations, and treatment of scombroid poisoning are reviewed separately. (See ["Marine toxins", section on 'Scombroid'](#).)

Several types of dark-meat fish (eg, tuna, bluefish, mackerel, and others) elaborate histamine-like chemicals during spoilage that are produced by bacteria in the fish flesh. Upon ingestion, these chemicals can cause reactions that mimic IgE-mediated allergy, with flushing and urticaria beginning within an hour of eating [5]. Symptoms that help distinguish these reactions from allergy include perioral sensations of tingling and burning, headache, and dizziness.

Diagnosis — Patients with scombroid poisoning do not have evidence of specific IgE to that type of fish. The absence of specific IgE may be demonstrated by skin prick testing with a different sample of the same type of fish, a commercial extract of that fish, or in vitro assays. Challenge with the seafood in question may be needed for conclusive diagnosis of scombroid poisoning.

Other approaches to diagnosis are possible if the patient saved or can obtain some of the fish that caused the reaction:

- A sample of the culprit fish can be analyzed for histamine content, as discussed separately. (See ["Marine toxins", section on 'Scombroid'](#).)
- A sample of the fish can be pulverized, and used in prick-by-prick skin testing and compared to the result with a commercial extract of the same fish. If only the culprit fish sample is positive, then it can be used to test a non-allergic volunteer [65]. If both individuals react positively to the culprit fish, then it can be deduced that histamine-like chemicals in the fish sample are the cause of these non-specific positive reactions, and the diagnosis is scombroid poisoning.

Other types of seafood poisoning — Other types of seafood poisoning (eg, toxins such as Ciguatoxin or contamination such as Botulism and others) may result in a variety of neurologic and gastrointestinal symptoms that usually do not resemble IgE-mediated allergic reactions [5]. The various forms of seafood poisoning are presented in detail elsewhere. (See ["Marine toxins"](#).)

However, diarrhetic shellfish poisoning (DSP) causes the delayed onset of nausea, vomiting, and colicky abdominal pain, and can mimic enterocolitis, as mentioned

previously. DSP results from the ingestion of mollusks contaminated with okadaic acid produced by dinoflagellates. This disorder generally comes to medical attention because of outbreaks. However, because DSP can be relatively mild and self-limited, it is unclear what proportion of cases is unreported.

CROSS-REACTIVITY — As previously mentioned, parvalbumins in fish and tropomyosins in shellfish are responsible for the majority of IgE-mediated allergies [22,23]. People with seafood allergy may react to these and/or to other seafood proteins. (See '[Pathogenesis](#)' above.)

Because the major allergenic proteins for fish and shellfish are different, individuals are usually allergic to one group or the other, although it is possible to be allergic to both. Allergy to both fish and shellfish was reported by approximately 10 percent of all those reporting any seafood allergy in the American telephone survey previously discussed [6]. One important limitation of this study is possible underestimation of cross-reactivity, since people with an initial reaction who subsequently avoid all seafood may report that they react to only one type. Formal challenge studies with sufficient numbers of people would be required to establish definite estimates.

Among persons with allergy to a fish or shellfish, approximately 30 to 50 percent will react clinically to more than one type of fish or shellfish [29,66]. Conversely, it is also possible to be allergic to just one specific type of fish or shellfish, such as tropical sole, swordfish, or one type of shrimp [67-69]. Patients in the latter group generally lack IgE antibodies to the major allergenic proteins and are presumed to be sensitized to a species-specific protein.

As is the case for many foods that share homologous proteins, sensitization (ie, positive allergy tests) to multiple species is more common than clinical reactivity (ie, the development of actual symptoms on ingestion). A Spanish study evaluated the relevance of sensitization to six regionally important species in 79 children with fish allergy [70]. While all subjects had positive skin tests to multiple species, only 39 percent had clinical reactions. Thus, positive test results alone are not sufficient to determine which related foods will cause symptoms.

Fish — Several studies have demonstrated that fish-allergic subjects often react to more than one type of fish, although this is not universal [29,71-73]. The following are representative:

- In the American telephone survey presented previously, reported reactions to multiple fish among those with any fish allergy was 67 percent [6]. Among the 58 individuals with fish allergy, 19 reported a reaction to only one type, 5 to two types, 13 to three to nine types, and the remainder was uncertain.
- Ten fish-allergic American children were evaluated with double-blind, placebo-

controlled oral food challenges (DBPCFCs) to between four and six different species of fish [2]. All reacted to at least one type, and three children reacted to more than one type.

- In a study of 20 codfish-allergic Italian children, positive skin tests to other fish were documented in 5 to 100 percent for each of nine species tested [74]. For those who ingested the fish to which antibody was detected, the clinical reaction rate per fish based upon history ranged from 25 to 100 percent. In these cod-allergic children, eel, bass, sole and tuna most frequently provoked reactions while salmon, sardine, and dogfish were least likely to induce symptoms.

In summary, a fish allergic patient is at high risk for reactions to other fish. There is insufficient data to predict which types of fish are more likely to be tolerated based upon the known allergy. In addition, skin testing or in vitro tests alone are often not sufficient to identify which types will cause clinical reaction.

Shellfish — It is also common for patients allergic to shellfish to react clinically to more than one type of shellfish. Extensive cross-reactivity among shellfish is explained by the fact that invertebrate tropomyosin is a pan allergen with significant sequence homology throughout many invertebrate species, including crustaceans, mollusks, squid, octopus, parasites, and non-marine insects (such as cockroaches, grasshoppers, and dust mites) [75-82]. However, there are clearly other factors that influence cross-reactivity, as homology cannot be used to predict an individual patient's sensitivity patterns. Invertebrate tropomyosins demonstrate less homology with vertebrate tropomyosins [83].

In the few studies examining cross-reactivity among foods within the crustacean or mollusk groups, sensitization was very high, and clinical reactivity was lower although very significant. The following studies provide information on these observations [6,78,84,85]:

- In 16 atopic, shrimp-allergic patients, greater than 80 percent had positive prick skin tests to crab, crayfish, and lobster [84]. Patients were not challenged to determine if they developed symptoms to the test-positive foods.
- In the American telephone survey, 232 people had allergy to shrimp, lobster, and/or crab [6]. Of these, 62 percent indicated allergy to one, 20 percent to two, and 18 percent to all three types. Thus, based on patient-provided history, nearly 40 percent of patients reacted to more than one type of crustacean.
- In a study evaluating nine patients with shrimp anaphylaxis, sera from all

patients reacted specifically with the tropomyosins of 13 crustaceans and mollusks [78]. However, patients were not challenged, so the clinical correlation is unclear.

- In the American telephone survey, 67 people reacted to scallops, clams, oysters, or mussels [6]. Of these, 51 percent reacted to just one type of mollusk, 19 percent to two, 8 percent to three, and 22 percent to all four types. In addition, 14 percent (41 persons) of those with shellfish allergy reported an allergy to both crustaceans and mollusks.

In summary, based upon limited data, up to 80 percent of patients with an allergy to one crustacean may be sensitized to other crustaceans, and approximately 40 percent may react clinically upon ingestion. Among mollusk-allergic patients, approximately 50 percent report reactions to more than one type of mollusk. Between 10 to 15 percent of patients allergic to any shellfish are allergic to both crustaceans and mollusks.

Cross-reactivity with non-food allergens — Invertebrate tropomyosin is also found in several non-marine allergenic organisms, such as dust mites and cockroaches. In a report of asthma induced by snail consumption in 28 patients, RAST inhibition studies indicated that house dust mite sensitization was the likely initial event, suggesting that sensitization by the respiratory route may predispose to the development of subsequent allergy upon seafood ingestion [80].

Several studies have implicated cross-reactivity between tropomyosins as responsible for the development of shellfish allergy in patients receiving immunotherapy for dust mite [86-88]. However, this phenomenon has not been adequately documented and other studies do not support the hypothesis. Myosin light chain in shrimp is homologous to an important allergen in cockroach, although the clinical significance of this is unknown [25].

There is no cross-reactivity between seafood allergens and radiocontrast media. This misconception is discussed elsewhere. (See "[Immediate hypersensitivity reactions to radiocontrast media](#)", section on 'Risk factors'.)

MANAGEMENT — The management of seafood allergy does not differ from that of other food allergies and requires instructions on avoidance and education about treatment of reactions in the event of accidental exposure.

Dietary recommendations

Avoidance — All patients must avoid the specific food that induced symptoms. In addition, general avoidance of all fish or all shellfish may be the safest and most practical strategy for people with severe reactions or reactions to multiple types of seafood.

Counseling about avoidance should include discussions about the following issues:

- **Cross-contact** — Patients must be counseled about accidental exposure to food allergens via cross-contact (ie, inadvertent exposure to the allergenic food by contamination of "safe" foods with small amounts of the culprit food). With seafood, this typically occurs at seafood counters, restaurants, and as a result of shared equipment (especially fryers). Reactions due to contact with contaminated saliva through kissing or sharing of utensils have also been reported [89].
- **Food labels** — Patients must read all food labels. Legislation has been enacted in the United States mandating that the ingredients labels on food packages plainly identify the presence of eight specified allergenic foods. These eight foods include fish and crustacean shellfish (as well as milk, eggs, tree nuts, peanuts, wheat, and soybeans) [90]. Mollusks are not included. This legislation applies to all foods packaged since January 2006, although foods labeled before January 2006 are still available in stores.
- **Unexpected and non-food sources** — Seafood components can appear in unexpected foods, as well as in non-food items. As an example, fish gelatin is a food additive derived from fish skin. The use of fish gelatin as a food additive is increasing in parallel with concerns over the risk of bovine spongiform encephalopathy with bovine gelatin [91]. Usual doses of fish gelatin are tolerated by most fish allergic persons, but anaphylactic reactions have been reported [91-93]. Results from one small series suggest that some individuals with fish allergy may tolerate fish oil supplements as well [94]. Medications, various health foods, and cosmetics may have ingredients derived from seafood, and labeling of non-food items is not strictly regulated.

Fish products can be used as clarifying (or fining) agents in the manufacture of some wines. However, available studies indicate that residual fining agents are unlikely to cause allergic reactions in fish allergic individuals. (See "[Food allergen avoidance](#)", [section on 'Alcoholic beverages'](#).)

- **Aerosolized seafood allergens** — Many of the allergenic proteins in seafood are stable and could be vaporized or released in steam during cooking. Although airborne exposures to food allergens are unlikely to cause anaphylaxis, respiratory reactions may occur from being near cooking fish or in fish markets [95,96].
- **Caution with anti-ulcer treatments** — Anti-ulcer drugs increase gastric pH and may impair digestion of food proteins. In a mouse model, anti-ulcer drugs were reported to predispose to allergic reactions to caviar caused by unstable

allergens that would be normally destroyed by digestion [43]. A human study included four codfish-allergic patients who underwent DBPCFC to codfish that was predigested at either pH 2 or pH 3 [97]. The codfish preparation digested at pH 3 produced symptoms in these patients at either a lower dose, or after a shorter time interval, compared to codfish digested at pH 2, suggesting that anti-ulcer therapy may place patients at increased risk for reactions to ingested seafood.

Eating other seafood — Seafood is obviously not an essential component of the diet, and the most straightforward approach in managing any food allergy is **complete** avoidance of the culprit food and all similar foods. This strategy would be logically expected to minimize the chances of accidental exposure of the culprit food through cross-contact.

However, there may be disadvantages to the strategy of avoiding all similar foods. There is some evidence, for example, that removing foods from the diet can increase the risk of becoming allergic to them. This appeared to be the case in a report of seven children with atopic conditions who were sensitized to fish but had no clinical symptoms on ingestion [98]. The children were placed on fish-elimination diets and followed prospectively. Within the ensuing two to five years, all of the children developed clinical allergy to fish, including two with anaphylaxis. Similar examples of this phenomenon exist for other foods [99]. Possible reasons for the heightened sensitivity include both lack of exposure and the opposite explanation, namely, ongoing low level exposure (through hidden sources or cross-contact).

Thus, if a patient with allergy to a certain fish or shellfish wishes to continue eating other forms of seafood, the clinician's recommendations must carefully balance the patient's preferences with what is known about cross-reactivity among seafood. The severity of the patient's reaction also influences the decision. (See '[Cross-reactivity](#)' above.)

The following scenarios illustrate some of the issues involved and our management approach. Individual clinicians may decide to adopt different strategies depending upon their level of expertise and the resources available (eg, ability to perform oral food challenges).

- For patients who have experienced life-threatening anaphylaxis to a specific shellfish, we advise avoidance of all shellfish, largely because of the higher chance of encountering a cross-reactive tropomyosin in these foods. Similarly, a person who reacted to one finned fish would usually be advised to avoid all finned fish. We typically do NOT advise patients with serious reactions to shellfish to avoid finned fish (or vice versa), since the major allergens in

shellfish and finned fish are different, as noted previously. However, patients must be wary of settings in which cross-contamination is common, such as seafood restaurants. It may be wise to avoid these settings altogether.

- For patients with non-life threatening reactions, we are more flexible in our approach. If patients are content to avoid all shellfish or finned fish (depending upon which group they reacted to), we do not discourage this approach. However, if a patient wishes to continue to include similar seafood in the diet, then a careful evaluation must be performed to determine which specific foods may be safely eaten. As an example, a patient who developed an allergy to codfish that is moderate in severity and has been avoiding all seafood for several months may ask about the safety of eating tuna, which had been a regular component of the patient's diet before the reaction.

In this case, we would first perform skin testing with commercial extracts of tuna. If negative, we would allow the ingestion of tuna because the experience in our clinic suggests the negative predictive value of skin prick testing for seafoods is generally high.

However, if there were any clinical suspicion of tuna allergy or if the clinician were uncomfortable proceeding without additional evaluation, skin testing and oral food challenge with fresh tuna should be performed. If skin tests were positive to tuna but the patient still had a strong interest in eating it, we would perform a cautious graded challenge to determine whether there was true clinical reactivity (because false-positive skin tests are not uncommon).

- We allow persons to continue to eat seafood that has not caused symptoms in the recent past, and which they have eaten regularly (similar to having just passed an oral food challenge). As an example, a patient with a newly diagnosed allergy to codfish who continued to eat tuna without incident after the reaction can simply continue to do so.

Management of reactions

IgE-mediated reactions — Identification of individuals with IgE-mediated seafood allergy is important because these reactions can be severe. As in other forms of food allergy, the severity of symptoms in a given individual may vary dramatically between reactions and the severity of an initial reaction should not be used to predict the patient's subsequent risk [100]. Accordingly, all individuals diagnosed with IgE-mediated seafood allergy should have an epinephrine autoinjector(s) available at all times [101]. Patients who have experienced anaphylaxis should have a written Anaphylaxis Action Plan. These measures are discussed in detail separately. (See "[Anaphylaxis: Rapid recognition and](#)

[treatment".](#))

Delayed gastrointestinal reactions — The management of children with food-protein induced enterocolitis caused by fish and other foods is presented in the specific topic review. (See "[Food protein-induced proctitis/colitis, enteropathy, and enterocolitis of infancy](#)".)

There are no data to guide recommendations about the treatment of delayed gastrointestinal reactions in adults, or the frequency with which patients require acute care. There are no reported fatalities from this disorder.

INFORMATION FOR PATIENTS — Educational materials on this topic are available for patients. (See "[Patient information: Food allergy symptoms and diagnosis](#)" and "[Patient information: Food allergy treatment and avoidance](#)".) We encourage you to print or e-mail these topic reviews, or to refer patients to our public web site, www.uptodate.com/patients, which includes these and other topics.

SUMMARY

Clinical features

- Allergy to fish or shellfish (crustaceans and mollusks) affects nearly 1 in 50 adults and is a leading cause of food-induced anaphylaxis. Fish is a common cause of food allergy in children, although rates of seafood allergy are lower than in adults. (See '[Introduction](#)' above and '[Epidemiology](#)' above.)
- Manifestations of IgE-mediated seafood allergy include urticaria/angioedema /anaphylaxis, occupational asthma, and food-dependent, exercise-induced anaphylaxis. IgE-mediated seafood allergy can be severe and is usually long-lasting. There are also non-IgE mediated forms of allergy that present with delayed gastrointestinal reactions, although limited data are available about these reactions. (See '[Clinical features](#)' above.)
- Parvalbumins in fish and tropomyosins in shellfish are the proteins that are responsible for the majority of IgE-mediated allergies. (See '[Pathogenesis](#)' above.)

Diagnosis and management

- Diagnosis of IgE-mediated seafood allergy is based upon a careful history supported by skin prick tests or in vitro tests for specific IgE. Positive tests for IgE may be present to seafood that is clinically tolerated, and a supervised oral food challenge may be necessary for definitive diagnosis. (See '[Diagnosis](#)' above.)
- Several factors may alter the allergenicity of seafood and complicate

diagnosis, including preparation method, changes as a result of digestion, and the specific part of the fish that is consumed ([table 2](#)). The differential diagnosis includes allergy to seafood parasites and non-allergic reactions to toxins in seafood. (See '[Diagnostic pitfalls](#)' above and '[Differential diagnosis](#)' above.)

- Rates of clinical cross-reactivity to different types of seafood within a group are high, ie, a person allergic to one fish is likely to react to others. In contrast, a minority (about 10 percent) of those allergic to any seafood are allergic to both fish and shellfish, although this observation is based on limited data. Because false positives on skin testing are possible, supervised challenge may be needed to definitely determine if a patient reacts to a specific seafood. (See '[Cross-reactivity](#)' above.)
- Management of seafood allergies includes instructions about avoidance of the specific culprit food, evaluations for reactivity to related foods in patients who wish to continue eating seafood, and education in the proper management of accidental exposures. (See '[Management](#)' above.)
- Patients with life-threatening reactions are generally advised to avoid all related seafood. Some patients will choose to avoid all seafood, to minimize the risk of exposure through cross-contact. (See '[Management](#)' above.)
- Among those with less severe reactions, some may wish to continue eating other forms of seafood in the future. In this case, testing and possibly oral challenges are needed to determine which specific foods are tolerated. (See '[Eating other seafood](#)' above.)
- All patients with IgE-mediated reactions to fish or shellfish should be equipped with epinephrine autoinjectors, regardless of the severity of their initial reactions. (See '[IgE-mediated reactions](#)' above.)

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GRAPHICS

Signs and symptoms of anaphylaxis

Skin:
Feeling of warmth, flushing [erythema], itching [may begin on palms and soles], urticaria, angioedema, morbilliform rash, and "hair standing on end" [piloerection]
Oral:
Itching or tingling of lips, tongue, or palate
Edema of lips, tongue, uvula, metallic taste
Gastrointestinal:
Nausea, abdominal pain [colic, cramps], vomiting [large amounts of "stringy" mucus], and diarrhea
Difficulty swallowing*
Respiratory:
Laryngeal - pruritus and "tightness" in the throat, dysphagia, dysphonia and hoarseness, and sensation of itching in the external auditory canals
Lung - shortness of breath, dyspnea, chest tightness, deep or repetitive cough, and wheezing
Nose - itching, congestion, rhinorrhea, and sneezing
Cardiovascular:
Feeling of faintness or dizziness; syncope, chest pain, palpitations, and/or hypotension (tunnel vision, difficulty hearing)
Neurologic:
Anxiety, apprehension, sense of impending doom, seizures, headache•, confusion
Ocular:
Periorbital itching, erythema and edema, tearing, and conjunctival erythema
Other:

Lower back pain due to uterine cramping in women

- * Often occurs in association with throat tightness and other upper airway symptoms.
- Not common in anaphylaxis overall; however, reported in up to 30 percent of patients with exercise-induced anaphylaxis.

Diagnostic considerations when evaluating fish and shellfish allergy

Concern	Implication/approach
Clinical cross-reactivity	The rate of serologic (positive test) cross reactivity exceeds the rate of true clinical reactivity, but both are high in seafood allergy. Therefore, caution is needed (evaluations with tests for IgE and possibly oral food challenges).
Overlap of symptoms with non-allergic seafood reactions	Spoilage of seafood most typically results in gastrointestinal reactions that are not consistent and do not mimic allergy (differentiated by history). However, spoilage of dark meat fish (scombroid poisoning) could result in symptoms that mimic allergy (pruritus, flushing).
Reactions may vary	Inconsistencies in reactions to fish could be attributable to manner of cooking or to which parts of the fish are eaten. Reduced digestion of fish protein is also a variable that could be altered if a patient takes antacid medication. These points should be examined in the history and considered during allergy testing.
Reactions may be attributed to seafood, but caused by other allergens	If a reaction occurs during a meal, ingredients must be reviewed to determine other causes (spices, etc). Other fish-related foods (caviar) or contaminants (parasites such as anisakis) could be causal

